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EXAMINER	
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ART UNIT	PAPER NUMBER
1634	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/806,899	PETROU ET AL.	
	Examiner	Art Unit	
	STEPHEN KAPUSHOC	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,26 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/05/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 26 and 27 are pending and examined on the merits.

Please note: The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This Office Action is in reply to Applicants' correspondence of 02/19/2009.

Applicants' remarks and amendments have been fully and carefully considered but are not found to be sufficient to put the application in condition for allowance. Any new grounds of rejection presented in this Office Action are necessitated by Applicants' amendments. Any rejections or objections not reiterated herein have been withdrawn in light of the amendments to the claims or as discussed in this Office Action.

This Action is made **FINAL**.

Response to Remarks Concerning Priority

1. Applicants have reiterated their arguments (p.6-7 of Remarks) in traversal of the Examiner's finding that the effective filing date of claims specifically requiring 'a regulatory region of the gene' (i.e.: as recited in claim 1 and relevant to claim 27 which depends from claim 1) is 3/23/2004, the filing date of the US Application. The Examiner has set forth that the claims include the language of screening for a mutation in 'a regulatory region' of the SCN1A gene, where the priority document does not support such a specific limitation. Applicants have argued that the Priority Document (i.e. Australian application 2003901425, dated 03/27/2003) discloses methods for testing a patient for SCN1A gene mutations, where the term 'gene' is believed to encompass both regulatory and non-regulatory regions. The Examiner maintains that the argument is not persuasive. While the generic term 'gene' may encompass different regions, portions, and sequence elements of the SCN1A genetic locus, the recitation of the

generic term is not a basis for the specific recitation of any one particular element. There is no contemplation or specific recitation in the Priority Document to single out 'a regulatory region' for the generically taught SCN1A gene. As such the Examiner maintains that because of the recitation of the required 'a regulatory region' in the claims, the effective filing date of the claims is the filing date of the US Application, which is 03/23/2004.

It is noted that new claim 26 does not recite 'a regulatory region of the gene', and as such the aforementioned particular issue related to priority is not germane to claim 26.

Withdrawn Claim Rejections - 35 USC § 112 2nd¶ - Indefiniteness

2. The rejection of claims 4 and 21 under 35 U.S.C. 112, second paragraph, as set forth on pages 5-7 of the Office Action of 08/19/2008, is **WITHDRAWN** in light of the cancellation of claims 4 and 21.

Withdrawn Claim Rejections - 35 USC § 112 1st¶ - Written Description

3. The rejection of claims 4 and 21 under 35 U.S.C. 112, first paragraph, as set forth on pages 7-10 of the Office Action of 08/19/2008, is **WITHDRAWN** in light of the cancellation of claims 4 and 21.

Withdrawn Claim Rejection - 35 USC § 112 1st¶ - Scope of Enablement

4. The rejection of claims 1, 2, 4, 21, 24, and 25 under 35 U.S.C. 112, first paragraph as lacking enablement in the full scope of the claims, as set forth on pages 10-17, is **WITHDRAWN** in light of the cancellation of claims and the amendments to the claims.

New Claim Rejections - 35 USC § 112 2nd ¶ - Written Description, New Matter

5. Claims 1, 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amended claims of 02/19/2009 recite the limitations 'has previously been detected in a patient clinically diagnosed with SMEI and is therefore considered SMEI associated' (in regard to an identified mutation) and 'the patient is categorized as having a very high probability of having SMEI when the mutation is SMEI associated'. Thus the claims require a categorization of a 'very high probability' of having SMEI when a detected mutation has previously been identified in an SMEI patient, and encompass any mutation (i.e. any substitution, insertion, or deletion of nucleotides). In so far as the specification as originally filed contemplates different degrees of likelihood for a subject to have SMEI, the categorization of 'very high probability' is only disclosed in association with the detection of de novo mutations that are 'truncation mutations' or 'result in a major disruption to the protein' (e.g.: Figure 1; p.5 lns.26-30). However the

instant claims require establishing a 'very high probability' for any mutation that has previously been detected in an SMEI patient. As such the required limitations of the amended claims encompass new matter.

Maintained Claim Rejections - 35 USC § 103 – Obviousness
Newly Applied as Necessitated by Amendments to the Claims

In the analysis of the claimed methods in view of the prior art it is noted that the methods have multiple steps which are conditional upon the results of previous steps of the claimed methods, as such these conditional steps are in fact optional given the specific results of performing the claimed method. For example, the limitations of the method as claimed in claim 1 are met by a method comprising screening for a mutation in the SCN1A gene, identifying the mutation, and establishing that the patient has a very high probability of having SMEI when a mutation is found that has previously been detected in a patient clinically diagnosed with SMEI. This portion of the independent claim is rendered obvious by the prior art, where the prior art is replete with references that provide the same analysis of SCN1A and SMEI patients as performed in the instant specification, and the prior art reaches the same conclusions as set forth in the specification, namely that certain de novo mutations in the SCN1A gene are identified in patients with SMEI and are associated with SMEI.

For example, in view of the teachings of Claes et al (as cited in the following rejection) it would be obvious for the skilled artisan to perform a method in which the SCN1A gene of a patient suspected of having SMEI is screened for a mutation by sequencing the gene (e.g.: relevant to step 1 of claim 1) and identification of the c.664C→T mutation (as disclosed in Table 2 of Claes et al as being a mutation in an SMEI patient) as a mutation that 'has previously been detected in a patient clinically diagnosed with SMEI and is therefore considered SMEI associated' results in a diagnosis of a very high probability of SMEI (relevant to part a of step 3 of claim 1).

Such a method, as rendered obvious by the teachings of Claes et al, satisfies the limitations of the rejected claims.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1, 26, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Claes et al (2001).

Claes et al teaches the analysis of mutations in the SCN1A gene and the relation of the mutations to SMEI.

Regarding claims 1 and 26, Claes et al teaches testing a patient sample for the existence of a mutation in the SCN1A gene (p.1329 – SCN1A mutation analysis), as required by step (1) of claims 1 and 26, and identifying the nature of the mutation as required by step (2) part (b) of claims 1 and 26(p. 1329 - Table 2). Relevant to step (3) and step (3)(a) of claims 1 and 26, the reference establishes that the particular mutations of Table 2 of the reference are detected in patients clinically diagnosed with SMEI, and thus are considered SMEI associated. Regarding the limitation of step (1) of claims 1 and 26, that the screening for the existence of an alteration is 'by sequencing the SCN1A gene', Claes et al teaches (p.1328 – Mutation detection and molecular–genetic analysis) that exons of the SCN1A gene were sequenced. Consistent with the

broadest reasonable interpretation of the requirement of 'sequencing the SCN1A gene', the sequence analysis of Claes et al is 'sequencing the SCN1A gene'.

Regarding claim 27, Claes et al teaches sequence analysis of the SCN1A gene using an ABI 3700 automated sequencer (p.1329, left col.), and that data was colleted and analyzed using ABI DAN sequence analysis software. The reference further demonstrates chromatograms (Fig 2) which indicate truncation mutations, where Claes et al teaches that 'in the majority of patients with SMEI, the mutation results in early termination of translation' (p.1330, right col.).

While Claes et al teaches the analysis of the SCN1A gene in patients, Claes et al does not *per se* perform a method of determining the likelihood that a patient suspected of having SMEI does have SMEI. However, it would be obvious to incorporate the teachings and conclusions of Claes et al to create the likelihood determination methods of the instant claims.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the explicit teachings of Claes et al to perform an analysis of a patient suspected of SMEI that meets the required limitations of the rejected claims. Given the teachings of Claes et al it would be obvious to screen for an alteration in the SCN1A gene of a patient where upon the identification of any of the mutations of Table 2 of Claes et al, the skilled artisan would recognize such a mutation as an alteration that has been previously detected in a patient clinically diagnosed with SMEI and provide a determination that there is a very high probability that such a patient has SMEI. One would be motivated to perform a method of

determining the likelihood that a patient suspected of having SMEI does or does not have SMEI using the techniques and teachings of Claes et al based on the teaching of Claes et al that particular mutations in the SCN1A gene are indicative of SMEI (p.1330 –Discussion) where the skilled artisan would recognize the diagnostic properties of identifying such a mutation in a patient.

Response to Remarks

Applicants have traversed the rejection of claims under 35 USC 103 as obvious in view of the teachings of Cleas et al. Applicants' arguments (p.11-14 of Remarks) have been fully and carefully considered but are not found to be persuasive to withdraw the rejection.

Applicants initially argue that (p.12-13 of Remarks) Claes et al does not teach or suggest ascertaining whether a detected mutation is SMEI associated or non-SMEI associated. The Examiner maintains that given the specific teachings of Claes et al with regard to particular mutations identified in SMEI patients, and the teachings of Claes et al that de novo mutations in SCN1A are probably a major cause of SMEI and that the majority of patients with SMEI have mutations that result in early termination of translation, the skilled artisan would recognize, that the identification in a patient suspected of having SMEI of any of the particular mutations taught by Claes et al would lead to the conclusion that the patient suspected of having SMEI has a very high probability of having SMEI. The skilled artisan in possession of the teachings of Claes et al would recognize the particular mutations as taught by Claes et al as, relevant to

the limitations of the claims, mutations previously detected in patients clinically diagnosed with SMEI and thus consider the mutations SMEI associated.

Applicants have argued that Claes et al does not teach that is an identified mutation is considered neither SMEI associated or non-SMEI associated, the next step is considering genetic data for the parents of the patient to determine if a mutation is de novo or inherited. This argument is not persuasive. The Examiner maintains that such a step is an optional step in the requirements of the claimed methods (i.e. the step is not performed when an SMEI associated mutation is identified). However, this step is in fact performed in the discovery analysis of Claes et al (e.g. p.1329-1330 – Results), where the reference in fact indicates that de novo mutations are probably a major cause of SMEI.

Applicants have argued that because the subjects of Claes et are were known to have SMEI, they would not have been classified based on their probability of having SMEI. This argument is not persuasive. In the instant rejection, the Examiner has maintained that the teachings of Claes et al renders obvious steps of the claimed methods; the rejection does not assert that Claes et al in fact classifies or categorizes SMEI probability, but that the skilled artisan with the teachings of Claes et al would arrive at the claimed methods of determining the likelihood that a patient suspected of having SMEI does or does not have SMEI.

Finally, while Applicants argue that the observations of Claes et al regarding 7 subjects known to have SMEI do not constitute an enabling reference to develop and carry out the claimed method, the Examiner maintains that the evidence of Claes et al

regarding SMEI associated SCN1A mutations is the same as that presented in the instant specification; both the cited prior art and the instant specification perform sequence analysis of individuals with SMEI to identify mutations in the SCN1A gene and establish that de novo SCN1A mutations are a likely cause of SMEI.

The rejection as set forth is **MAINTAINED.**

Conclusion

8. No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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/Stephen Kapushoc/
Art Unit 1634